

What is claimed is:

1. A method for changing a target nucleic acid sequence, the method comprising:
  - a) providing nucleic acid target in a form that can be replicated by a polymerase devoid of the proof-reading function;
  - b) contacting said replicable form of the nucleic acid target with said polymerase under conditions sufficient for template-directed nucleic acid synthesis in a living cell; and
  - c) recovering nucleic acid synthesis products, whose nucleotide sequence differs from the initial target sequence by at least one nucleotide.
2. The method according to claim 1, wherein said nucleic acid target encodes a polypeptide.
- 15 3. The method according to claim 1 or 2, wherein said polymerase is an RNA-dependent RNA polymerase.
4. The method according to any one of claims 1 to 3, wherein said polymerase is an RNA-dependent DNA polymerase.
- 20 5. The method according to any one of the preceding claims, wherein the nucleic acid synthesis products are recovered after selecting and/or screening nucleic acid synthesis products based on their properties.
6. The method according to any one of the preceding claims, wherein said nucleic acid synthesis products are recovered after one or several rounds of selection and/or screening.
7. The method according to any one of the preceding claims, wherein the method is specifically used for changing properties of proteins or nucleic acids in a desired manner.
- 30 8. The method according to any one of the preceding claims, wherein the polymerase is a genetically modified or wild-type polymerase.

9. The method according to any one of the preceding claims, wherein the RNA virus or other RNA replicon is genetically modified or wild-type.
- 5           10. The method according to any one of the preceding claims, wherein the nucleic acid target is operably linked with determinants essential for detectable replication by the polymerase.
- 10           11. The method according to any one of the preceding claims, wherein the nucleic acid target is incorporated into the genome of an RNA virus or another RNA replicon, such as RNA virus-like particle, viroid or RNA-based autonomous genetic element.
- 15           12. The method according to claim 11, wherein the RNA virus or RNA replicon encodes the polymerase.
13. The method according to any one of the preceding claims, wherein the nucleic acid encoding the polymerase and the target nucleic acid are distinct nucleic acids.
- 20           14. The method according to any one of the preceding claims, wherein the nucleic acid target is a nucleic acid having detectable biological activity, preferably selected from the group comprising enzymatic, regulatory and specific binding activity.
- 25           15. The method according to any one of the preceding claims, wherein the nucleic acid target encodes a protein having detectable biological activity, preferably selected from the group comprising enzymatic, regulatory and specific binding activity.
- 30           16. The method according to any one of the preceding claims, wherein the nucleic acid target is RNA.
17. The method according to any one of the preceding claims, wherein the nucleic acid target is DNA.

18. The method according to any one of the preceding claims, wherein the nucleic acid synthesis products are RNA molecules.
- 5           19. The method according any one of the preceding claims, wherein the nucleic acid synthesis products are DNA molecules.
- 10          20. The method according any one of the preceding claims, wherein the polymerase originates from an RNA virus or other RNA replicon.
- 15          21. The method according any one of the preceding claims, wherein the polymerase originates from an RNA bacteriophage.
- 20          22. The method according to claim 20 or 21, wherein the polymerase originates from a member of the *Cystoviridae* family, preferably from a bacteriophage selected from the group comprising  $\phi$ 6,  $\phi$ 7,  $\phi$ 8,  $\phi$ 9,  $\phi$ 10,  $\phi$ 11,  $\phi$ 12,  $\phi$ 13 and  $\phi$ 14, most preferably from bacteriophage  $\phi$ 6.
- 25          23. The method according to any one of the preceding claims, wherein the replicable form of the nucleic acid target is contacted with the polymerase in a prokaryotic cell, preferably in a gram-negative bacterial cell, more preferably in a bacterial cell selected from the group comprising *Pseudomonas sp.*, *Escherichia sp.* and *Salmonella sp.*, most preferably in a cell of *Pseudomonas syringae*.
- 30          24. The method according to any one of claims 1 to 22, wherein the replicable form of the nucleic acid target is contacted with the polymerase in a eukaryotic cell, such as mammalian, insect, plant or yeast cell.
- 35          25. The method according to any one of the preceding claims, wherein the nucleic acid target is delivered into the living cell by using a suicide vector, preferably a DNA vector, most preferably a DNA plasmid.
26. The method according to any one of the preceding claims, wherein a suicide vector, comprising a target nucleic acid operably linked with sequences sufficient for detectable replication by the viral replication apparatus, is used to incorporate said nucleic acid target into the genome of said RNA virus.

27. A living cell system for changing a target nucleic acid sequence, which comprises
- a target nucleic acid sequence operably linked with determinants essential for replication by an RNA synthesis apparatus of an RNA virus or another RNA replicon;
  - a living cell capable of supporting the replication of the RNA virus or other RNA replicon; and
  - a selection/screening procedure for selecting/screening a change in the properties of the nucleic acid synthesis products.
28. The cell system according to claim 27, wherein the RNA-synthesis apparatus is from a member of *Cystoviridae* family.
29. The cell system according to claim 27 or 28, wherein the living cells are bacteria, preferably gram-negative bacteria, more preferably bacteria selected from the group comprising *Pseudomonas* sp., *Escherichia* sp. and *Salmonella* sp., most preferably *Pseudomonas syringae*.
30. The cell system according to any one of claims 27 to 29, wherein the cells are carrier-state cells or can be transformed into carrier state.
31. A kit for changing nucleic acid or protein sequences, which comprises:
- a) a vector for transient expression of target nucleic acid in preselected cells that either are carrier-state or can be transformed into carrier state and/or
  - b) a genetically modified virus into where the target nucleic acid can be introduced; and/or
  - c) cells that either are carrier-state or can be transformed into carrier state.